REMARKS

Entry of the foregoing amendment and favorable consideration of the subject application is respectfully requested in view of the following comments.

Claims 1-9 are currently pending in the subject application. By the foregoing amendment, claim 1 has been amended to incorporate limitations from original claims 2 and 3 therein, and claims 2 and 3 have been cancelled.

Specifically, claim 1 has been amended to more positively recite a medical instrument for transdermally administering a medicine comprising a bag and an ionic medicine or an ionic medicine-containing substance sealed in the bag, wherein the bag comprises an anion exchange membrane and a cation exchange membrane which are melt-adhered to each other along the peripheral edges thereof.

Applicants respectfully submit that no new matter has been entered in this amendment and that the subject application is in condition for allowance.

Rejection of Claims 1-9 under 35 U.S.C. § 103(a)

The Office Action rejects claims 1-9 under 35 U.S.C. § 103(a) as being unpatentable over Matsumura, et al., U.S. Pub. No. 2005/0070840A1, in view of Kedem, et al., U.S. 4,217,200, and further in view of Theeuwes, et al., U.S. 5,169,382. The Office

Action states:

The Matsumura et al reference discloses an iontophoresis device that has an working electrode 11 connected to a medical instrument (13, 14, 15), consisting of a anion-exchange membrane & a cation-exchange membrane connected to a ionic medicine, and a counter electrode 21 connected to the working electrode 11 through a cell 3 and utilizes a electrolyte layer 12 to connect the working electrode 11 to a medical instrument (13,14,15). Now even though Matsumura does not explicitly disclose the medical instrument comprising a bag attention is directed to Theeuwes et al. The Theeuwes reference teaches an iontophoresis device that utilizes an ionic medicine which can be sealed in a bag, see col. 11 lines 41-47. Therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to modify the device of Matsumura et al with the device of Theeuwes in order to provide an efficient, disposable, and/or interchangeable drug reservoir for use with iontophoresis. Noweven though Matsumura does not explicitly disclose the use of utilizing an ion-exchange membrane bag attention is directed to Kedem. The Kedem reference teaches the use of anion-exchange membrane & cation-exchange membrane bags see col. 1 line 35- col. 2 line 26. Therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to modify the device of Matsumura with the device of Kedem in order to provide a convenient disposable and/or interchangeable medical instrument.

With respect to claims 2 & 3, wherein the "... by melt-adhering ..." is deemed to be written in product by process language and since the bag is sealed it would inherently be able to have been sealed by that process, also it would be obvious for one of ordinary skill in the art to utilize melt-adhering to seal and form the bag since it is well known to do so not just in the medical art but also generally in sealing bags.

With respect to claim 4, wherein the ionic-medicine substance is a sheet impregnated with a solution of an ionic medicine, see para [00121] Matsumura.

With respect to claim 7, now even though the device of Matsumura does not explicitly disclose the use of a flexible armoring member for the electrodes attention is directed to Theeuwes. The Theeuwes

> reference teaches a flexible armoring member 22 in figure 1 on the device. Therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to modify the device of Matsumura with the device of Theeuwes in order to provide a flexible protecting member for protecting the components of the device from damage.
>
> With respect to claims 8-9, wherein the electrolyte layer connects the working electrode to the medical instrument, see figures 3 & 4 Matsumura, and wherein the layer is in the form of a paste or a gel, see para [0122] Matsumura.

Applicants respectfully traverse the rejection because the prima *facie case* of obviousness has not been established with respect to the presently pending claims 1-9.

The Federal Circuit has ruled that a *prima facie* case of obviousness must establish: (1) some suggestion or motivation to modify the references; (2) a reasonable expectation of success; and (3) that the prior art references teach or suggest all claim limitations. Amgen, Inc. v. Chugai Pharm. Co., 18 USPQ2d 1016, 1023 (Feb. Cir. 1991); In re Fine, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988); In re Wilson, 165 USPQ 494, 496 (C.C.P.A. 1970).

A *prima facie* case of obviousness must also include a showing of the reasons why it would be obvious to modify the references to produce the present invention. See Ex parte Clapp, 277 USPQ 972, 973 (Bd. Pat. App. & Inter. 1985). The examiner bears the initial burden to provide some convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings. Id. at 974.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established as there is no convincing line of reasoning which would lead one of ordinary skill in the art to apply the teachings of Kedem or Theeuwes to modify the device of Matsumura, et al., to obtain the iontophoresis device of the present claims.

Although disclosing a basic structure of an iontophoresis device, Matsumura does not describe or suggest sealing an ionic medicine in a bag comprising an anion exchange membrane and a cation exchange membrane sealed as recited in the present claims.

In the present invention, an ionic medicine is sealed in a bag which comprises an anion exchange membrane and a cation membrane wherein the membranes are sealed to each other along their peripheral edges by melt adhering. In this manner, the medicine necessary for iontophoresis and the ion exchange membrane are provided as a single, compact structure which is portable and easily handled. Furthermore, since the bag containing the medicine is formed from the ion exchange membrane, a separate ion exchange structure between the bag and the patient's skin is not necessary thereby permitting the transdermal instrument to more favorably conform to the patient's skin for effective administration of the medicine.

Matsumura merely discloses stacked layers of membrane bodies and fails to disclose or suggest the structure of the present

claims comprising a sealed bag containing an ionic medicine for transdermal administration.

The examiner contends that, because Theeuwes, et al., teaches an iontophoresis device that utilizes an ionic medicine which can be sealed in a bag, it would be obvious to one of ordinary skill in the art to modify the device of Matsumura, et al., with the device of Theeuwes, et al., to provide an efficient, disposable, and/or interchangeable drug reservoir for use with iontophoresis.

In this regard, Applicants point out that Theeuwes, et al., may disclose a flexible bag sealing a medicine therein, but that bag is not disclosed as being made from an anion exchange membrane and a cation exchange membrane which are melt adhered to each other along their peripheries. If it were, then the separate ion exchange membrane 30 between the bag and the patient's skin required by Theeuwes, et al., would not be necessary.

The examiner refers specifically to col. 11, lines 41-47 of Theeuwes, et al., and Applicants respectfully point out that this portion of the disclosure of the reference refers to the structure shown in Fig. 3 of Theeuwes, et al.

> "FIG. 3 illustrates another type of electrotransport system 36 suitable for use with the composite membrane 30 of this invention. System 36 has an agent reservoir 38 which can be in the form of a flexible bag as shown or a matrix as in system 10; a first current conducting membrane 40 positioned between reservoir 38 and battery 42; and a second current conducting member 44 positioned between reservoir 38 and a conductive backing member 46. The system has an insulating member 48 and a peripheral ion-conducting adhesive 50. The system is packaged with

> a strippable release liner 52. Suitable system materials are disclosed in U.S. Pat. No. 4,713,050, incorporated herein by reference (Col. 11, lines 39-51)."

Thus, Theeuwes, et al., discloses a structure that is inconsistent with the device of the present invention. Theeuwes, et al., requires the presence of the composite membrane 30 which is disclosed as exhibiting larger electrically-assisted transport than passive. As Theeuwes, et al., states:

> "This invention is a composite membrane having properties of both types of membranes wherein a hydrophilic resin, such as an ion exchange resin, is blended into a hydrophobic polymeric matrix. The resin has a high permeability for agent and provides a complex of 'microporous' ion exchange pathways. The hydrophobic polymer has a low permeability for agent and provides a non-permeable hydrophobic matrix structure (Col. 5, lines 36-43)."

The composite membrane of Theeuwes, et al., reduces or eliminates the passive transport of ionic compounds while maintaining a low electrical resistance. Thus, the composite membrane 30 of Theeuwes, et al, is the ion exchange membrane of the device whereas the reservoir 38 is merely made from materials disclosed in U.S. Patent 4,713,050, Sibalis, which are described as "... a pouch containing the drug of choice in solution or suspension, the walls of which are sufficiently dense to prevent leakage of the drug under ambient conditions, but sufficiently porous to permit the migration of the charged particles or ions under the influence of the electric field imposed." That language neither discloses nor

requires that the walls of the reservoir 38 of Theeuwes, et al., be made from "an anionic exchange membrane and a cation exchange membrane which are melt-adhered to each other along the peripheral edges thereof" as recited in the present claims. If the reservoir 38 of Theeuwes, et al., had the structure of the bag as claimed herein, the composite membrane 30 of Theeuwes, et al., would not be necessary.

Furthermore, if Matsumura, et al., were modified according to the teaching of Theeuwes, et al., it would follow that the material of the stacked membranes of Matsumura, et al. would have to be changed to conform to the teachings of Theeuwes, et al., thereby requiring the inclusion in Matsumura, et al., of the composite membrane 30 of Theeuwes, et al., which is not the case in the present invention.

Accordingly, absent some suggestion in Theeuwes, et al., that the composite membrane 30 would not be necessary, Applicants respectfully submit that it would not be obvious to modify the device of Matsumura, et al., according to the teachings of Theeuwes, et al., as suggested by the examiner.

With regard to Kedem, et al., the examiner contends that this reference teaches the use of anion exchange membrane and cation exchange membrane bags, citing col. 1, line 35-col. 2, line 26, and that it would be obvious to one of ordinary skill in the art to modify the device of Matsumura, et al., with the device of Kadem in

order to provide a convenient disposable and/or interchangeable medical instrument.

Applicants respectfully point out that the device of Kadem, et al., consists of a type of membrane unit for use in electrodialysis and desalination devices. As such, they essentially constitute filtration units and require an entrance and an exit as is clearly noted in the Summary of the Invention referred to by the examiner. Indeed, Kadem further discloses that the membranes form "... an integral unit with a frame, which frame is characterized in that it can be attached by heat-sealing to similar frames of other membranes ..." (Col. 1, lines 37-40). Thus, Kedem requires structure that is inconsistent with an iontophoresis device, i.e., a frame about the peripheral edges between the membranes and inlet and outlet structures to permit the flow of dialysate through the cells formed from the framed membrane structures. Accordingly the structure and purpose of Kedem, et al. is different from the device as recited in the present claims and Applicants respectfully submit that it would not be obvious to apply the teachings of Kadem, et al., as employed in a device relying on a counter-current flow of dialysate and electrolyte through a filtration unit to an iontophoretic device for direct transdermal administration of medicine to a patient.

With regard to the rejection of claims 2 and 3, Applicants respectfully submit that the cancellation of claims 2 and 3 has

rendered the examiner's rejection moot.

As to the rejection of claim 7, Applicants respectfully submit that, since this claim is ultimately dependent from claim 1 as requiring the device recited therein, the examiner's rejection is traversed for the reasons given above. As noted above, Theeuwes, et al., discloses a significantly different structure than disclosed by Matusmura, et al., or the present application, and having a specific purpose not encountered by either Matsumura, et al. or the present invention. Accordingly, modification of Matsumura, et al., as suggested by the examiner would neither be obvious, under the present conditions, nor would it result in the device of the present invention.

Similarly, claims 8 and 9 of the present invention require the structure of claim 1 which structure is not disclosed or suggested by Matsumura, et al., nor, for the reasons already presented, would modification of Matsumura, et al., be obvious to one of ordinary skill in the art from the teachings of Theeuwes, et al., or Kadem, et al., to achieve the device as claimed in claims 8 and 9 herein.

Accordingly, Applicants respectfully submit that the rejection of claims 1-9 as unpatentable over Matsumura, et al., in view of Theeuwes, et al., and Kadem, et al., is not supported by the references and should be withdrawn.

Claims 1-5 are further rejected under 35 U.S.C. 103(a) as being unpatentable over Kedem et al (US Patent No.4217200) in

view of Theeuwes et al (US Patent No. 5169382). The Office Action states:

> The Kedem reference discloses a medical instrument comprising a bag made of an ion-exchange membrane which can be heat sealed together and can be formed of an anion-exchange membrane and of a cation-exchange membrane, see col. 1 line 35- col. 2 line 26. Now even thought Kedem et al does not explicitly disclose the use of an ionic medicine or a sheet or a film impregnated with a solution of an ionic medicine used for iontophoresis attention is directed to Theeuwes et al. The Theeuwes et al reference teaches an iontophoresis device that utilizes an ionic medicine which can be sealed in a bag, see col. 11 lines 41-47. therefore, it would be obvious to one of ordinary skill in the art at the time of the invention to modify the device of Kedem with the device of Theeuwes in order to provide an efficient, disposable, and/or interchangeable drug reservoir for use with iontophoresis.
>
> With respect to claims 2 & 3, wherein the "... by melt-adhering ..." is deemed to be written in product by process language and since the bag is sealed it would inherently be able to have been sealed by that process, also it would be obvious for one of ordinary skill in the art to utilize melt-adhering to seal and form the bag since it is well known to do so not just in the medical art but also generally in sealing bags.
>
> With respect to claim 4, wherein the ionic medicine-containing substance is a sheet or a film impregnated with a solution of an ionic medicine, it is well known in the art to impregnate anionic medicine in a sheet or a film in order to provide a stable solid delivery form.

Applicants respectfully traverse the rejection because the prima *facie case* of obviousness has not been established with respect to the presently pending claims 1-5.

Applicants respectfully point out that, as previously noted, the device of Kadem, et al., consists of a type of membrane unit

for use in electrodialysis and desalination devices. As such, they essentially constitute filtration units and require an entrance and an exit as is clearly noted in the Summary of the Invention referred to by the examiner. Indeed, Kadem further discloses that the membranes form "... an integral unit with a frame, which frame is characterized in that it can be attached by heat-sealing to similar frames of other membranes ..." (Col. 1, lines 37-40). Thus, Kedem requires structure that is inconsistent with an iontophoresis device, i.e., a frame about the peripheral edges between the membranes and inlet and outlet structures to permit the flow of dialysate through the cells formed from the framed membrane structures. Accordingly the structure and purpose of Kedem, et al. is different from the device as recited in the present claims.

The examiner contends that, because Theeuwes, et al., teaches an iontophoresis device that utilizes an ionic medicine which can be sealed in a bag, it would be obvious to one of ordinary skill in the art to modify the device of Kedem, et al., with the device of Theeuwes, et al., to provide an efficient, disposable, and/or interchangeable drug reservoir for use with iontophoresis.

In this regard, Applicants point out that Theeuwes, et al., may disclose a flexible bag sealing a medicine therein, but that bag is not disclosed as being made from an anion exchange membrane and a cation exchange membrane which are melt adhered to each other along their peripheries. If it were, then the separate ion

exchange membrane 30 between the bag and the patient's skin required by Theeuwes, et al., would not be necessary.

The examiner refers specifically to col. 11, lines 41-47 of Theeuwes, et al., and Applicants respectfully point out that this portion of the disclosure of the reference refers to the structure shown in Fig. 3 of Theeuwes, et al.

> "FIG. 3 illustrates another type of electrotransport system 36 suitable for use with the composite membrane 30 of this invention. System 36 has an agent reservoir 38 which can be in the form of a flexible bag as shown or a matrix as in system 10; a first current conducting membrane 40 positioned between reservoir 38 and battery 42; and a second current conducting member 44 positioned between reservoir 38 and a conductive backing member 46. The system has an insulating member 48 and a peripheral ion-conducting adhesive 50. The system is packaged with a strippable release liner 52. Suitable system materials are disclosed in U.S. Pat. No. 4,713,050, incorporated herein by reference (Col. 11, lines 39-51)."

Thus, Theeuwes, et al., discloses a structure that is inconsistent with the device of the present invention. Theeuwes, et al., requires the presence of the composite membrane 30 which is disclosed as exhibiting larger electrically-assisted transport than passive. As Theeuwes, et al., states:

> "This invention is a composite membrane having properties of both types of membranes wherein a hydrophilic resin, such as an ion exchange resin, is blended into a hydrophobic polymeric matrix. The resin has a high permeability for agent and provides a complex of 'microporous' ion exchange pathways. The hydrophobic polymer has a low permeability for agent and provides a non-permeable hydrophobic matrix structure (Col. 5, lines 36-43)."

The composite membrane of Theeuwes, et al., reduces or eliminates the passive transport of ionic compounds while maintaining a low electrical resistance. Thus, the composite membrane 30 of Theeuwes, et al, is the ion exchange membrane of the device whereas the reservoir 38 is merely made from materials disclosed in U.S. Patent 4,713,050, Sibalis, which are described as "... a pouch containing the drug of choice in solution or suspension, the walls of which are sufficiently dense to prevent leakage of the drug under ambient conditions, but sufficiently porous to permit the migration of the charged particles or ions under the influence of the electric field imposed." That language neither discloses nor requires that the walls of the reservoir 38 of Theeuwes, et al., be made from "an anionic exchange membrane and a cation exchange membrane which are melt-adhered to each other along the peripheral edges thereof" as recited in the present claims. If the reservoir 38 of Theeuwes, et al., had the structure of the bag as claimed herein, the composite membrane 30 of Theeuwes, et al., would not be necessary.

Furthermore, if Kadem, et al., were modified according to the teaching of Theeuwes, et al., it would follow that the material of the membranes of Kadem, et al. would have to be changed to conform to the teachings of Theeuwes, et al., thereby requiring the inclusion in Kadem, et al., of the composite membrane 30 of Theeuwes, et al., which is not the case in the present invention.

Accordingly, absent some suggestion in Theeuwes, et al., that the composite membrane 30 would not be necessary, Applicants respectfully submit that it would not be obvious to modify the device of Kadem, et al., according to the teachings of Theeuwes, et al., as suggested by the examiner.

Furthermore, Applicants respectfully submit that it would not be obvious to apply the teachings of Kadem, et al., as employed in a device relying on a counter-current flow of dialysate and electrolyte through a filtration unit to an iontophoretic device for direct transdermal administration of medicine to a patient. In addition, it is not seen how modification of Kadem, et al., to provide an ionic medicine or a sheet or film impregnated with a solution of an ionic medicine used for iontophoresis as used in Theeuwes, et al., would be obvious when the purpose of the Kadeem, et al., device is completely different from the transdermal administration of medicine to a patient.

Applicants therefore respectfully submit that it would not be obvious to one of ordinary skill in the art to modify the electrodialysis apparatus of Kadem, et al., according to the teachings of Theeuwes, et al., to obtain the iontophoretic device of the present invention.

With regard to the rejection of claims 2 and 3, Applicants respectfully submit that the cancellation of claims 2 and 3 has rendered the examiner's rejection moot.

As for the rejection of claim 4, the present invention requires the structure of claim 1 which structure is not disclosed or suggested by Kadem, et al., nor, for the reasons already presented, would modification of Kadem, et al., be obvious to one of ordinary skill in the art from the teachings of Theeuwes, et al., to achieve the device as claimed in claim 7, since it would fundamentally change the device of Kadeem, et al., to something neither disclosed nor intended by that reference.

Accordingly, Applicants respectfully submit that the rejection of claims 1-5 as unpatentable over Kadem, et al., in view of Theeuwes, et al., is not supported by the references and should be withdrawn.

In light of the foregoing, Applicants submit that a prima facie case of obviousness has not been sufficiently established in the present application and that the application is now in condition for allowance. The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of the pending claims and allow the pending claims. Favorable action with an early allowance of the claims pending is earnestly solicited.

Respectfully submitted,

SHERMAN & ASSOCIATES

Attorney for Applicants
Robert L. Haines
Reg. No. 35,533

SHERMAN & ASSOCIATES
415 N. Alfred Street
Alexandria, Virginia 22314
703-549-2282